

**ABSTRACT OF THE DISCLOSURE**

The present invention concerns methods and reagents useful in modulating BACE gene expression in a variety of applications, including use in therapeutic, diagnostic, target validation, and genomic discovery applications. Specifically, the invention relates to small  
5 nucleic acid molecules, such as short interfering nucleic acid (siNA), short interfering RNA (siRNA), double-stranded RNA (dsRNA), micro-RNA (miRNA), and short hairpin RNA (shRNA) molecules capable of mediating RNA interference (RNAi) against beta-secretase (BACE), amyloid precursor protein (APP), pin-1, presenillin 1 (PS-1) and/or presenillin 2 (PS-2) gene expression and/or activity. The small nucleic acid molecules are useful in the  
10 treatment of Alzheimer's disease and any other condition that responds to modulation of BACE, APP, pin-1, PS-1 and/or PS-2 expression or activity.